PATENT COOPERATION TREATY

	From the INTERNATIONAL BUREAU
PCT	То:
NOTIFICATION OF ELECTION (PCT Rule 61.2)	Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ÉTATS-UNIS D'AMÉRIQUE
Date of mailing: 10 September 1999 (10.09.99)	in its capacity as elected Office
International application No.: PCT/JP99/01080	Applicant's or agent's file reference: YCT-395
International filling date: 05 March 1999 (05.03.99)	Priority date: 06 March 1998 (06.03.98)
Applicant: SUMIDA, Shuji et al	
in the demand filed with the International preliminan 05 March 1999 in a notice effecting later election filed with the International preliminan 7. The election X was was not	o (05.03.99) mational Bureau on:
made before the expiration of 19 months from the priority Rule 32.2(b).	and on, mile and our applica, main the time mile and
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer: J. Zahra Telephone No.: (41-22) 338.83.38
	2027200

PCT

世界知的所有権機関 国際事務局 特許協力条約に基づいて公開された国際出願



(51) 国際特許分類6	A1	(11) 国際公開番号		WO99/44630
A61K 38/17		(43) 国際公開日	•	1999年9月10日(10.09.99)

(21) 国際出願番号

PCT/JP99/01080

(22) 国際出願日

1999年3月5日(05.03.99)

(30) 優先権データ 特願平10/54799

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(81) 指定国 AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, 欧州特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許 (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG), ARIPO特許 (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)

添付公開書類

国際調査報告書

(54)Title: PROTEIN-FREE PREPARATIONS

(54)発明の名称 蛋白非添加製剤

(57) Abstract
Stable preparations containing granulocyte colony stimulating factor which contain the granulocyte colony stimulating factor and 1 part by weight or less, per 1 part by weight of the granulocyte colony stimulating factor, of at least 1 pharmaceutically acceptable surfactant and have a pH value of 7 or lower.

Applicant's or agent's file reference

International application No.

YCT-395

PCT/JP99/01080

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

	A/416)
International filing date (day/month/year) Priority date (day/mont 05 March 1999 (05.03.99) 06 March 1998	•

Intermetional Potent Classification (IPC) or national alongification	- 4 IDC
International Patent Classification (IPC) or national classification at A61K 38/17	nd IPC
AUTR 30/17	
×	
Applicant CHUGALSEIVAKII I	KABUSHIKI KAISHA
 This international preliminary examination report has been and is transmitted to the applicant according to Article 36. 	prepared by this International Preliminary Examining Authority
2. This REPORT consists of a total of5 sheets	s, including this cover sheet
	sheets of the description, claims and/or drawings which have been ets containing rectifications made before this Authority (see Rule tions under the PCT).
These annexes consist of a total of	sheets.
3. This report contains indications relating to the following ite	ems:
I Basis of the report	
II Priority	
III Non-establishment of opinion with regard t	to novelty, inventive step and industrial applicability
IV Lack of unity of invention	
V Reasoned statement under Article 35(2) wi citations and explanations supporting such	th regard to novelty, inventive step or industrial applicability; statement
VI Certain documents cited	·
"	
VII Certain defects in the international applicat	ion
VIII Certain observations on the international ap	pplication
Date of submission of the demand	Date of completion of this report
05 March 1999 (05.03.99)	30 September 1999 (30.09.1999)
Name and mailing address of the IPEA/JP	Authorized officer
·	

Date of submission of the demand	Date of completion of this report
05 March 1999 (05.03.99)	30 September 1999 (30.09.1999)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

International application No.

PCT/JP99/01080

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

I.	Basis	of the report
1.	With	regard to the elements of the international application:*
	\boxtimes	the international application as originally filed
		the description:
	ـــا	pages, as originally filed
		pages, filed with the demand
		pages, filed with the letter of
	Ш	the claims:
		pages, as originally filed
		pages, as amended (together with any statement under Article 19 pages, filed with the demand
		, med with the fetter of
i		the drawings:
		pages, as originally filed
		pages, filed with the demand
		pages, filed with the letter of
!		he sequence listing part of the description:
		pages, as originally filed
		pages, filed with the demand
		pages, filed with the letter of,
		the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
		or 55.3).
3.	With prelir	regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international minary examination was carried out on the basis of the sequence listing:
	Ц	contained in the international application in written form.
	Щ	filed together with the international application in computer readable form.
	Ц	furnished subsequently to this Authority in written form.
	Ц	furnished subsequently to this Authority in computer readable form.
		The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
İ		The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
1.		The amendments have resulted in the cancellation of:
		the description, pages
		the claims, Nos.
		the drawings, sheets/fig
;.		This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**
i.	in this and 70	,
* /	4ny re	eplacement sheet containing such amendments must be referred to under item I and annexed to this report.

'INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP 99/01080

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
 citations and explanations supporting such statement

Statement			
Novelty (N)	Claims	4,5	YES
	Claims	1-3, 6-12	NO
Inventive step (IS)	Claims		YES
4	Claims	1-12	NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims		NO

- 2. Citations and explanations
 - Claims 1-3 and 6-12

Document 1, Claim 7, discloses an aqueous pharmacological preparation which contains a therapeutically effective quantity of granulocyte colony stimulating factor and a quantity of surfactant no greater than the quantity of granulocyte colony stimulating factor employed, and which does not contain protein as a stabilizer. Examples 4, 5 and 7-9 further describe preparations which contain polysorbate(80) as a surfactant at more than 0.2 part by weight to 1 part by weight of granulocyte colony stimulating factor, and do not contain protein as a stabilizer.

Document 2, in Claims 10 which refers back to Claims 1, 2 and 8, discloses storage-ready pharmaceutical preparations containing granulocyte colony stimulating factor for use as a liquid injection or infusion, to which at least one preservative is added at a concentration of up to 2% during the production of the preparation, although this can be omitted if desired, with benzalkonium chloride, widely used as a surfactant, included as a possible preservative, wherein the pH of the preparation is approximately 2.0 to approximately 7.4. In Examples 6-9 it describes preparations which do not contain protein as

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP 99/01080

a stabilizer, in which the ratio of recombinant human granulocyte stimulating factor and polysorbate(80) is 7:2.

Document 3, Claim 2, discloses freeze-dried preparations which further include a physiologically permissible surfactant at less than the quantity of granulocyte colony stimulating factor employed, or at most the same quantity; and Claim 11 indicates that the pH of pharmacological preparations in the form of aqueous solutions obtained by redissolving the freeze-dried preparations in Claim 2 is 6.5-8 or 3-5. Moreover, Example 10 describes a preparation in which Tween 80 and polysorbate(80) exceed 0.2 parts by weight to 1 part by weight of granulocyte colony stimulating factor and which do not contain protein as a stabilizer.

All of the preparations described in these examples are the same as the invention according to Claims 1-3, 6-8 and 12.

Therefore, Claims 1-3, 6-8 and 12 are not novel because they are disclosed in Documents 1 to 3.

Claims 4 and 5

Documents 1 to 3 do not disclose the invention as described in Claims 4 and 5, wherein there is 0.4-0.8 parts by weight of surfactant to 1 part by weight of granulocyte colony stimulating factor.

However, the fact that this ratio of ingredients is suitable when it comes to producing preparations does not go beyond the conventional wisdom of a person skilled in the art. Therefore, given the disclosures in Documents 1 to 3, setting a suitable ratio of granulocyte colony stimulating factor and surfactant, and a suitable pH value, is not especially difficult for a person skilled in the art.

Therefore, Claims 4 and 5 do not involve an inventive step.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP 99/01080

Document 1 : JP, 8-505610, A

Document 2 : JP, 6-510031, A

Document 3 : JP, 8-504784, A

特 許 協 力 条 約

発信人 日本国特許庁(国際予備審査機関)

出願人代理人

社 本 一 夫

PCT

あて名

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(法施行規則第57条) (PCT規則71.1)

発送日

(日.月.年)

12.10.99

出願人又は代理人の書類記号

YCT-395

重要な通知

国際出願番号

際出願番号 PCT/JP99/01080 国際出願日

(日.月.年) 05.03.99

優先日

(日.月.年) 06.03.98

出願人(氏名又は名称)

中外製薬株式会社

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選択官庁が適用する期間及び要件の詳細については、PCT出願人の手引き第Ⅱ巻を参照すること。

名称及びあて名

日本国特許庁 (IPEA/JP) 郵便番号100-8915 東京都千代田区霞が関三丁目4番3号 権限のある職員

特 許 庁 長 官

4C 9736

電話番号 03-3581-1101 内線 3452

(添付用紙の注意書きを参照)

PCT

国際予備審査報告

(法第12条、法施行規則第56条) [PCT36条及びPCT規則70]

出願人又は代理人 の書類記号 YCT-395	今後の手続きについては、国際予備審査報告の送付通知(様式PCT/ IPEA/416)を参照すること。
国際出願番号 PCT/JP99/01080	国際出願日 (日.月.年) 05.03.99 優先日 (日.月.年) 06.03.98
国際特許分類 (IPC) Int.Cl ^o A 6 1 I	38/17
出願人 (氏名又は名称) 中	外 製 薬 株 式 会 社
1. 国際予備審査機関が作成したこの	国際予備審査報告を法施行規則第57条(PCT36条)の規定に従い送付する。
2. この国際予備審査報告は、この表	紙を含めて全部で 4 ページからなる。 が属書類、つまり補正されて、この報告の基礎とされた及び/又はこの国際予備審
	む明細書、請求の範囲及び/又は図面も添付されている。 実施細則第607号参照)
3. この国際予備審査報告は、次の内	容を含む。
I X 国際予備審査報告の基礎	
Ⅱ	

新規性、進歩性又は産業上の利用可能性についての国際予備審査報告の不作成

国際予備審査の請求書を受理した日 05.03.99	国際予備審査報告を作成した日 30.09.99	
名称及びあて先	特許庁審査官(権限のある職員)	4C 9736
日本国特許庁(IPEA/JP) 郵便番号100-8915 東京都千代田区霞が関三丁目4番3号	瀬 下 浩 一	
2020 Bit 1 1415 E1524 124 - 1 H - 1	電話番号 03-3581-1101 内線	3 4 5 2

PCT35条(2)に規定する新規性、進歩性又は産業上の利用可能性についての見解、それを裏付けるため

□ 発明の単一性の欠如

の文献及び説明 ある種の引用文献

国際出願の不備

国際出願に対する意見

I. 国際予備審査報告の基礎	
1. この国際予備審査報告は下記の出願書類に基づいて作成さ 応答するために提出された差し替え用紙は、この報告書に PCT規則70.16,70.17)	れた。 (法第6条 (PCT14条) の規定に基づく命令において「出願時」とし、本報告書には添付しない。
X 出願時の国際出願書類	
明細告 第 ページ、 明細告 第 ページ、 明細告 第 ページ、	出願時に提出されたもの 国際予備審査の請求 書と共に提出されたもの 付の書簡と共に提出されたもの
請求の範囲 第 項、 請求の範囲 第 項、 請求の範囲 第 項、 請求の範囲 第 項、	出願時に提出されたもの PCT19条の規定に基づき補正されたもの 国際予備審査の請求郡と共に提出されたもの 付の書簡と共に提出されたもの
図面 第 ページ/図、 図面 第 ページ/図、 図面 第 ページ/図、	国際予備審査の請求書と共に提出されたもの
明細書の配列表の部分 第 ページ、明細書の配列表の部分 第 ページ、明細書の配列表の部分 第 ページ、明細書の配列表の部分 第 ページ、	出願時に提出されたもの 国際予備審査の請求書と共に提出されたもの 一一一一一一一一一一一一一一一一一一一一一一一一一一一一一一一一一一一一
2. 上記の出願書類の言語は、下記に示す場合を除くほか、こ	の国際出願の言語である。
	たは55.3にいう翻訳文の言語 おり、次の配列表に基づき国際予備審査報告を行った。 ないよる配列表 是出された番面による配列表
4. 補正により、下記の書類が削除された。	ジ/図 が出願時における開示の範囲を越えてされたものと認めら 。(PCT規則70.2(c) この補正を含む差し替え用紙は上 1告に添付する。)

国際予備審査報告	!	国際出願番号	PCT/JP99/	01080
V. 新規性、進歩性又は産業上の利用可能性に 文献及び説明	こついての法第12彡	Ř (PCT35∮	₹(2)) に定める見解、 	それを裏付ける
1. 見解		,		
新規性(N)	請求の範囲 請求の範囲		4, 5 1-3, 6-12	
進歩性(IS)	請求の範囲 請求の範囲		1-12	有 無
産業上の利用可能性 (IA)	請求の範囲 請求の範囲		1-12	有 無
	·			
2. 文献及び説明 (PCT規則70.7) ○請求の範囲1-3, 6-12に 文献1の請求項7には、治療的 顆粒球コロニー刺激因子の量以「パク質を含有しない水性薬理製剤	りに有効な量の Fの量の界面活 flが記載されて	性剤を含有 いる。また	し、安定化剤と 、実施例4 , 5	. 7-9に
おいては界面活性剤としてのポリ 0.2重量部を越え、かつ安定) ノルベート80 L剤としてのタ	か親私球コンパク質を	ローー 刺放囚丁 含有しないもの	が記載され

ている。 文献 2 の請求項 1、2 及び 8 を受ける請求項 1 0 には、注射又は注入溶液として使用するための顆粒球コロニー刺激因子を含有する保存処理された医薬製剤であって、該医薬製剤の製造中に少なくとも 1 種の保存剤を 2 %までの濃度で添加し、所望により除去してもよいものであり、保存剤として界面活性剤として広く用いられる塩化ベンザルコニウムを含み、pHが約2.0~約7.4であるものが記載されている。そして、実施例 6 - 9 には組換えヒト顆粒球コロニー刺激因子とポリソルベート 8 0 との比が 7:2 であって安定化剤としてのタンパク質を含有しない溶液が記載されている。

文献3の請求項2には、使用している顆粒球コロニー刺激因子の量より少ない又は最大でそれと同量である生理学的に寛容される界面活性剤を更に含む凍結乾燥製剤が記載されており、また請求項11には、請求項2に記載の凍結乾燥製剤の再溶解により得られる水溶薬理製剤のpH値が $6.5\sim8$ 又は $3\sim5$ のものが記載されている。さらに実施例10には、界面活性剤としてTween 80及びポリソルベート80が顆粒球コロニー刺激因子に対して0.2重量部を越え、かつ安定化剤としてのタンパク質を含有しないものが記載されている。

」ないものが記載されている。 そして、これらの実施例に記載されているものは、いずれも本願の請求の範囲1− 3、6−8及び12に係る発明とは同一である。

3、6~6及び12に除る発列とは同じなる。 従って、請求の範囲1-3、6-8及び12は文献1ないし3に記載されているから新規性を有さない。

○請求の範囲4,5について 文献1ないし3には、請求の範囲4及び5の発明である、界面活性剤が顆粒球コロニー刺激因子に対して0.4~0.8重量部であるものが記載されていない。しかしながら、製剤の製造に際し、その成分比などの値を適当な値とすることは当業者が通常認識する程度の事項であるにすぎないから、文献1ないし3の記載に基づき、顆粒球コロニー刺激因子と界面活性剤の比率及び製剤のpHの値を適宜設定することは、当業者にとって格別困難な事項であるとはいえない。 従って、請求の範囲4及び5は、進歩性を有さない。

国際予備審査報告

国際出願番号 PCT/JP99/01080

補充欄 (いずれかの欄の大きさが足りない場合に使用すること)

第 V 棡の続き

文献1:JP, 8-505610, A 文献2:JP, 6-510031, A 文献3:JP, 8-504784, A

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

SHAMOTO, Ichio Yuasa and Hara Section 206, New Ohtemachi Building 2-1, Ohtemachi 2-chome Chiyoda-ku Tokyo 100-0004 **JAPON**

IMPORTANT NOTIFICATION
International filing date (day/month/year) 05 March 1999 (05.03.99)
Priority date (day/month/year) 06 March 1998 (06.03.98)

CHUGAI SEIYAKU KABUSHIKI KAISHA et al

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date

Priority application No.

Country or regional Office or PCT receiving Office

Date of receipt of priority document

06 Marc 1998 (06.03.98)

10/54799

JP

26 Apri 1999 (26.04.99)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Marc Salzman

Telephone No. (41-22) 338.83.38

Facsimile No. (41-22) 740.14.35

PATENT COOPERATION TREATY 09/622 48 7 1080

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

SHAMOTO, Ichio Yuasa and Hara Section 206, New Ohtemachi Building 2-1, Ohtemachi 2-chome Chivoda-ku Tokyo 100-0004 **JAPON**

Date of mailing (day/month/year)

10 September 1999 (10.09.99)

Applicant's or agent's file reference

YCT-395

IMPORTANT NOTICE

International application No.

PCT/JP99/01080

International filing date (day/month/year) 05 March 1999 (05.03.99)

Priority date (day/month/year) 06 March 1998 (06.03.98)

Applicant

CHUGAI SEIYAKU KABUSHIKI KAISHA et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice: AU, CN, EP, IL, JP, KR, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,ES,FI,GB,GD,GE,GH,GM,HR,HU, ID,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,SD,

SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZW The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 10 September 1999 (10.09.99) under No. WO 99/44630

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

J. Zahra

Telephone No. (41-22) 338.83.38

Facsimile No. (41-22) 740.14.35

2828572

PATENT COOPERATION TREATY 09/622487

PCT

INFORMATION CONCERNING ELECTED OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

From the INTERNATIONAL BUREAU

SHAMOTO, Ichio Yuasa and Hara Section 206, New Ohtemachi Building 2-1, Ohtemachi 2-chome Chiyoda-ku Tokyo 100-0004 JAPON

Date of mailing (day/month/year)

10 September 1999 (10.09.99)

Applicant's or agent's file reference

International application No.

PCT/JP99/01080

YCT-395

IMPORTANT INFORMATION

International filing date (day/month/year) 05 March 1999 (05.03.99)

Priority date (day/month/year) 06 March 1998 (06.03.98)

Applicant

CHUGAI SEIYAKU KABUSHIKI KAISHA et al

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

AP :GH,GM,KE,LS,MW,SD,SL,SZ,UG,ZW

EP:AT,BE,CH,CY,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE

National :AU,BG,BR,CA,CN,CZ,DE,GB,IL,JP,KR,MN,NO,NZ,PL,RO,RU,SE,SK,US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

EA:AM,AZ,BY,KG,KZ,MD,RU,TJ,TM

OA:BF,BJ,CF,CG,CI,CM,GA,GN,GW,ML,MR,NE,SN,TD,TG

National :AL,AM,AT,AZ,BA,BB,BY,CH,CU,DK,EE,ES,FI,GD,GE,GH,GM,HR,HU,ID,IN,

IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MW,MX,PT,SD,SG,SI,SL,TJ,TM,TR,

TT,UA,UG,UZ,VN,YU,ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing a translation of any translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer:

J. Zahra

Telephone No. (41-22) 338.83.38

Facsimile No. (41-22) 740.14.35

PCT

REQUEST

For receiving Office	use only
International Application No.	
International Filing Date	5/3/99
Name of receiving Office and "PCT Int	ernational Application"

·						
The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.	Name of receiving Office and "PCT International Application"					
	Applicant's or agent's file reference (if desired) (12 characters maximum) YCT-3					
Box No. I TITLE OF INVENTION						
PROTEIN-FREE FORMULATIONS						
Box No. II APPLICANT						
Name and address: (Family name followed by given name; for a designation. The address must include postal code and name of co address indicated in this Box is the applicant's State (that is, country of residence is indicated below.)		This person is also inventor.				
CHUGAI SEIYAKU KABUSHIKI KAISHA	·	Telephone No.				
5-1, Ukima 5-chome, Kita-ku,		Facsimile No.				
Tokyo 115-8543 Japan	·					
		Teleprinter No.				
State (that is, country) of nationality:	State (that is, country) of Japan	residence:				
Japan This person is applicant all designated all	ed States except the	United States the States indicated in				
for the purposes of: States V the United	States of America of .	America only the Supplemental Box				
Box No. III FURTHER APPLICANT(S) AND/OR (FURT		· · · · · · · · · · · · · · · · · · ·				
Name and address: (Family name followed by given name; for a designation. The address must include postal code and name of co address indicated in this Box is the applicant's State (that is, country of residence is indicated below.)	n tegal entity, full official unity. The country of the y) of residence if no State	This person is:				
SUMIDA, Shuji		TT applicant and inventor				
c/o Chugai Seiyaku Kabushiki K	aisha	v applicant and inventor				
41-8, Takada 3-chome, Toshima-	ku,	inventor only (If this check-box is marked, do not fill in below.)				
Tokyo 171-8545 Japan						
State (that is, country) of nationality: Japan	State (that is, country) of Japan	residence:				
		United States America only the States indicated in the Supplemental Box				
V Further applicants and/or (further) inventors are indicated	on a continuation sheet.					
Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE						
The person identified below is hereby/has been appointed to act of the applicant(s) before the competent International Authoritie	on behalf s as: V a	gent common representative				
Name and address: (Family name followed by given name, for designation. The address must include postal of	a legal entity, full official code and name of country.)	Telephone No.				
SHAMOTO, Ichio, (8970) Patent A	ttorney	(03)3270-6641				
YUASA AND HARA, Section 206, New		Facsimile No.				
Bldg., 2-1, Ohtemachi 2-chome,	Chiyoda-ku,	(03) 3246-0233				
Tokyo 100-0004 Japan		Teleprinter No.				
Address for correspondence: Most this sheet has where	no agent or common repres	entative is/has been appointed and the				
Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.						

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Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)							
If none of the	he following sub-b	oxes is used, thi	s sheet should	not be in	cluded in the request.		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) SATO, Yasushi					This person is: applicant only		
c/o Chugai Sei		V applicant and inventor					
					inventor only (If this check-box		
41-8, Takada 3-chome, Toshima-ku, inventor only (If this check-box is marked, do not fill in below.) Tokyo 171-8545 Japan							
State (that is, country) of nation Japan	ality:		State (that is, co	-	residence:		
This person is applicant for the purposes of:	all designated States	all designated the United Stat	States except tes of America		United States America only the States indicated in the Supplemental Box		
Name and address: (Family no designation. The address must address indicated in this Box is of residence is indicated below	ine applicant s siale	en name; for a le and name of coun e (that is, country)	gal entity, full of try. The country of residence if no	official of the State	This person is:		
	,		•		applicant and inventor		
- 10				*-	inventor only (If this check-box is marked, do not fill in below.)		
••		*		-	· ·		
State (that is, country) of nation	nality:		State (that is, c	ountry) of	residence:		
This person is applicant for the purposes of:	all designated States	all designated the United Stat	States except les of America		United States America only the States indicated in the Supplemental Box		
Name and address: (Family no designation. The address must address indicated in this Box is of residence is indicated below	the applicant's State				This person is:		
					applicant and inventor		
14		· .			inventor only (If this check-box is marked, do not fill in below.)		
State (that is, country) of natio	nality:	`	State (that is, o	country) of	residence:		
This person is applicant for the purposes of:	all designated States	all designated the United Sta	States except ates of America		e United States		
Name and address: (Family n designation. The address mus address indicated in this Box is of residence is indicated below	i include postal code sthe applicant's Stat				This person is:		
	·				applicant and inventor		
·					inventor only (If this check-box is marked, do not fill in below.)		
State (that is, country) of nation	nality:		State (that is, o	country) of	residence:		
This person is applicant for the purposes of:	all designated States		States except ates of America		the States indicated in the Supplemental Box		
Further applicants and	or (further) invente	ors are indicated o	n another conti	nuation sh	ncet.		

Box N	o.V	DESIGNATION OF STATES					
The fo	The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):						
Dagio	nal Pa	atent			•		
<u>V</u>	AP	ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, LIG Uganda, ZW Zimbahwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT					
\(\sqrt{1}	EA	Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT					
V	EP	European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT					
⊻	The state of the s						
Notice	al Data	aesirea, specify on doued line) int (if other kind of protection or treatment desired, specify or	n dott	ed line	y:		
Nation		United Arab Emirates	☑		Liberia		
		Albania	\square		Lesotho		
_		Armenia	$\overline{\square}$		Lithuania		
[<u>V</u>]		Austria	∇		Luxembourg		
		Australia	∇		Latvia		
<u> </u>		Azerbaijan	$\overline{\Omega}$		Republic of Moldova		
		Bosnia and Herzegovina			Madagascar		
V V		Barbados	$\overline{\mathbb{Q}}$	MK	The former Yugoslav Republic of Macedonia		
		Bulgaria	لک	. ,4114	The former Tugoslav Republic of Manageresia		
	BR		☑	MN	Mongolia		
		Belarus			Malawi		
		Canada	\square		Mexico		
		and LI Switzerland and Liechtenstein	∇		Norway		
		China	∇		New Zealand		
		Cuba	Ø.		Poland		
		Czech Republic			Portugal		
		Germany	$\overline{\mathbf{v}}$		Romania		
		Denmark	$\overline{\square}$		Russian Federation		
		Estonia		SD	Sudan		
	ES	Spain	∇	SE	Sweden		
	Fi	Finland		SG	Singapore		
		United Kingdom	$\overline{\mathbf{v}}$	SI	Slovenia		
		Grenada	$\overline{\mathbf{v}}$	SK	Slovakia		
V		Georgia	∇		Sierra Leone		
		Ghana	$\overline{\nabla}$	TJ	Tajikistan		
		1 Gambia	∇	TM	Turkmenistan		
	HR	Croatia	∇	TR	Turkey		
	HU		∇	TT	Trinidad and Tobago		
	lD	Indonesia	$\overline{\nabla}$	UA	Ukraine		
V		Israel	図	UG	Uganda		
		India	∇	us	United States of America		
	IS	Iceland		•			
		Japan	⑦		Uzbekistan		
			V		Viet Nam		
		Kyrgyzstan	∇		Yugoslavia		
				ZA	South Africa		
			∇	ZW	Zimbabwe		
	KR	Republic of Korea	Ch	eck-b	oxes reserved for designating States which have		
		Z Kazakhstan	bec	come I	party to the PC1 after issuance of this sheet.		
		C Saint Lucia					
1	LK	Sri Lanka					
P		nory Designation Statement: In addition to the design	ation				

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) another designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Supplemental Box If the Supplemental Box is not used, this sheet should not be included in the request.

- 1. If, in any of the Boxes, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:
 - (i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all design ated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;
- (iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;
- (vi) if, in Box No. 17, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. 17" and indicate for each additional earlier application the same type of information as required in Box No. 17;
- (vii) if, in Box No. 17, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. 17", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed.
- 2. If, with regard to the precautionary designation statement contained in Box No. 1', the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.
- 3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.

"Continuation of Box No. IV"

The same address as Box IV

IMAI, Shosuke, (7112) Patent Attorney
MASUI, Chuji, (7669) Patent Attorney
KURITA, Tadahiko, (7523) Patent Attorney
KOBAYASHI, Yasushi, (7527) Patent Attorney
EJIRI, Hiroko, (9163) Patent Attorney

Sheet No. ...5....

Box No. VI PRIORITY C	Tox No. VI PRIORITY CLAIM Further priority claims are indicated in the Supplemental Box.							
Filing date Number			Where earlier application is:					
of earlier application (day/month/year)	of earlier application		national application: regional application: in regional Office		international application: receiving Office			
item (1) 6/3/1998	54799/19	54799/1998		Japan				
item (2)								
item (3)								
The receiving Office is recoff the earlier application()					(1)			
* Where the earlier application is Convention for the Protection of It	ADIDO amplication		mdatam to indicate in th	e Supplemental Rox at least of	ne country party to the Paris upplemental Box.			
	NAL SEARCHING	G AUT	HORITY					
Choice of International Searce (if two or more International Secompetent to carry out the intern	arching Authorities ar ational search, indicat	e sear	ch has been carried out l	earlier search; reference oy or requested from the Interna Number	e to that search (if an earlier ational Searching Authority): Country (or regional Office)			
the Authority chosen; the two-letter ISA / JP	code may be usea) :	Dat	e (day/month/year)	Number	Country (or regional 2)			
Box No. VIII CHECK LIST	T; LANGUAGE O	F FILI	NG					
This international application of the following number of shee	contains This inte	mation	al application is accon	panied by the item(s) mark	ked below:			
request :	5 1. [V] 1e		lation sheet	· ·				
description (excluding	2. [V] se	-	signed power of attorn		, , , , , , , , , , , , , , , , , , ,			
sequence listing part) :	I —			ney; reference number, if an	ıy.			
claims	2 (—		t explaining lack of sig					
abstract	- -			in Box No. VI as item(s):				
drawings :				lication into (language):	at a trial and an atomical			
sequence listing part of description				g deposited microorganism				
or description .	8. 🔲 ու	ucleotid	le and/or amino acid s	equence listing in computer	readable form			
Total number of sheets:	22 9. 🔽 ot				<u>-</u>			
Figure of the drawings which should accompany the abstract	t:	int	inguage of filing of the ternational application	Japanese	· · · · · · · · · · · · · · · · · · ·			
Box No. IX SIGNATURE	OF APPLICANT	OR AC	ENT	(C. 1	wie of from moding the vernest			
Next to each signature, indicate the n	ame of the person signing	g and the	capacity in which the perso	on signs (if such capacity is not ob	vious from reading the requesty.			
SHAMOTO, IC	hio. (8970) Pa	atent Attorr	ney	•			
IMAI, Shosu	ke, (7112)	Pat	ent Attorne	y '				
MASUI, Chuj	i, (7669)	Pate	ent Attorney	7				
KURITA, Tad	lahiko, (75	23)	Patent Atto	rney	* *			
KOBAYASHI, Yasushi, (7527) Patent Attorney								
EJIRI, Hiroko, (9163) Patent Attorney								
For receiving Office use only								
Date of actual receipt of the purported international application: 2. Drawings:								
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:								
4. Date of timely receipt of the corrections under PCT Ar	he required ticle 11(2):		-		not received:			
5. International Searching At (if two or more are compe	uthority ICA / T	P	6. Tran	smittal of search copy delay search fee is paid.	/ed			
		For Inte	ernational Bureau use	only				
Date of receipt of the record by the International Bureau:	сору							